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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Laurence Hermitte

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05/09/2008

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EXAMINER

WESTERBERG, NISSA M

ART UNIT

PAPER NUMBER

1618

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/565,442	<b>Applicant(s)</b> HERMITTE ET AL.	
	<b>Examiner</b> Nissa M. Westerberg	<b>Art Unit</b> 1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 29 February 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 12 - 31 is/are pending in the application.
- 4a) Of the above claim(s) 14, 18 - 20, 22, 24, 27, 30 and 31 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 12, 13, 15 - 17, 21, 23, 25, 26, 28 and 29 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 05 July 2006 is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>1/20/06; 4/12/06</u>  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Election/Restrictions***

1. Applicant's election with traverse of group I with hyaluronic acid as the polymer and divinylsulfone as the cross linking agent in the reply filed on November 26, 2007 and non-polymeric chains grafted chains in the reply filed February 29, 2008 is acknowledged. The traversal is on the grounds that the claimed invention is drawn to a matrix and not to the selection of a single polymer as the biocompatible polymers constitute a class of compounds currently used. Applicant believes that the special technical feature is the grafting of the various grafted chains that protects the matrix from degradation.

These arguments are not found to be persuasive. While the claims are drawn to a matrix material, the properties of the matrix are determined by the constituents of that matrix. Applicant has not rebutted how the believed special technical feature is not known in the prior art and therefore the feature in common between all the groups does represent a contribution over the prior art and therefore can constitute a special technical feature.

The requirement is still deemed proper and is therefore made FINAL.

### ***Specification***

The instant application has one figure but the specification does not contain a brief description of the drawings. The preferred content and arrangement of the specification is provided below.

#### **Content of Specification**

- (a) Title of the Invention: See 37 CFR 1.72(a) and MPEP § 606. The title of the invention should be placed at the top of the first page of the specification unless the title is provided in an application data sheet. The title of the invention should be brief but technically accurate and descriptive, preferably from two to seven words may not contain more than 500 characters.
- (b) Cross-References to Related Applications: See 37 CFR 1.78 and MPEP § 201.11.
- (c) Statement Regarding Federally Sponsored Research and Development: See MPEP § 310.
- (d) The Names Of The Parties To A Joint Research Agreement: See 37 CFR 1.71(g).
- (e) Incorporation-By-Reference Of Material Submitted On a Compact Disc: The specification is required to include an incorporation-by-reference of electronic documents that are to become part of the permanent United States Patent and Trademark Office records in the file of a patent application. See 37 CFR 1.52(e) and MPEP § 608.05. Computer program listings (37 CFR 1.96(c)), "Sequence Listings" (37 CFR 1.821(c)), and tables having more than 50 pages of text were permitted as electronic documents on compact discs beginning on September 8, 2000.
- (f) Background of the Invention: See MPEP § 608.01(c). The specification should set forth the Background of the Invention in two parts:
  - (1) Field of the Invention: A statement of the field of art to which the invention pertains. This statement may include a paraphrasing of

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the applicable U.S. patent classification definitions of the subject matter of the claimed invention. This item may also be titled "Technical Field."

- (2) Description of the Related Art including information disclosed under 37 CFR 1.97 and 37 CFR 1.98: A description of the related art known to the applicant and including, if applicable, references to specific related art and problems involved in the prior art which are solved by the applicant's invention. This item may also be titled "Background Art."
- (g) Brief Summary of the Invention: See MPEP § 608.01(d). A brief summary or general statement of the invention as set forth in 37 CFR 1.73. The summary is separate and distinct from the abstract and is directed toward the invention rather than the disclosure as a whole. The summary may point out the advantages of the invention or how it solves problems previously existent in the prior art (and preferably indicated in the Background of the Invention). In chemical cases it should point out in general terms the utility of the invention. If possible, the nature and gist of the invention or the inventive concept should be set forth. Objects of the invention should be treated briefly and only to the extent that they contribute to an understanding of the invention.
- (h) Brief Description of the Several Views of the Drawing(s): See MPEP § 608.01(f). A reference to and brief description of the drawing(s) as set forth in 37 CFR 1.74.
- (i) Detailed Description of the Invention: See MPEP § 608.01(g). A description of the preferred embodiment(s) of the invention as required in 37 CFR 1.71. The description should be as short and specific as is necessary to describe the invention adequately and accurately. Where elements or groups of elements, compounds, and processes, which are conventional and generally widely known in the field of the invention described and their exact nature or type is not necessary for an understanding and use of the invention by a person skilled in the art, they should not be described in detail. However, where particularly complicated subject matter is involved or where the elements, compounds, or processes may not be commonly or widely known in the field, the specification should refer to another patent or readily available publication which adequately describes the subject matter.
- (j) Claim or Claims: See 37 CFR 1.75 and MPEP § 608.01(m). The claim or claims must commence on separate sheet or electronic page (37 CFR 1.52(b)(3)). Where a claim sets forth a plurality of elements or steps, each element or step of the claim should be separated by a line indentation.

There may be plural indentations to further segregate subcombinations or related steps. See 37 CFR 1.75 and MPEP § 608.01(i)-(p).

- (k) Abstract of the Disclosure: See MPEP § 608.01(f). A brief narrative of the disclosure as a whole in a single paragraph of 150 words or less commencing on a separate sheet following the claims. In an international application which has entered the national stage (37 CFR 1.491(b)), the applicant need not submit an abstract commencing on a separate sheet if an abstract was published with the international application under PCT Article 21. The abstract that appears on the cover page of the pamphlet published by the International Bureau (IB) of the World Intellectual Property Organization (WIPO) is the abstract that will be used by the USPTO. See MPEP § 1893.03(e).
- (l) Sequence Listing. See 37 CFR 1.821-1.825 and MPEP §§ 2421-2431. The requirement for a sequence listing applies to all sequences disclosed in a given application, whether the sequences are claimed or not. See MPEP § 2421.02.

### ***Claim Objections***

2. Claim 29 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 16 requires the presence of antioxidant agents, vitamins and other dispersed pharmacological agents. This group of items is joined by “and” and is not in Markush format, so all three items listed are required to be present. In dependent claim 29, the matrix is only required to contain one element, either vitamins or other dispersed pharmacologically active agents.

### ***Double Patenting***

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 12, 13, 15 – 17, 21, 23, 25, 26, 28 and 29 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 10 and 11 of copending Application No. 10/588,186. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 10 and 11 of '186 are generic to all that is recited in claims 12, 13, 15 – 17, 21, 23, 25, 26, 28 and 29 of the instant application. That is, claims 12, 13, 15 – 17, 21, 23, 25, 26, 28 and 29 of the instant application falls entirely within the scope of claims 10 and 11 of '186. Specifically, the claims of '186 recite a product made by a process in which a cross linking agent, such as divinylsulfone, and a biocompatible polymer, such as hyaluronic acid, are allowed to react and then an additional quantity of polymer is added to the polymerization reaction so as to decrease the overall concentration of polymer and cross linking agent. The product produced by this process comprises cross linked biocompatible polymer that can optional contain at least one dispersed active ingredient.

The claims of the instant application recite a matrix comprised of biocompatible polymer, such as hyaluronic acid, a cross linking agent, such as divinylsulfone and a grafted side chain. This matrix can optional contain other active ingredients such as antioxidants, vitamins and/or other pharmacologically active ingredients.



This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

***Claim Rejections - 35 USC § 112 1<sup>st</sup> Paragraph***

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 12, 13, 15 – 17, 21, 23, 25, 26, 28 and 29 are rejected under 35

U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 12 contains the phrase “non-polymeric chains having antioxidant properties or properties for inhibiting reactions of degradation of said matrix” (lines 10 – 12). Examples of chains possessing properties for inhibiting reactions of degradation of said matrix of vitamins, enzymes or cyclic molecules are given in the specification (p 8, ln 21 – 23). Vitamins, enzymes and cyclic molecules are large genera that encompass highly variant members with a myriad of possibilities. The specification provides insufficient written description as to what types of activity is necessary to inhibit degradation of the polymer matrix. For examples, do all cyclic molecules prevent matrix degradation or are certain size rings and/or chemical compositions (e.g., certain

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heterocyclic rings) required in order to degradation to be inhibited? Therefore, Applicant has not met the written description provision for grafted chains with properties for inhibiting reactions of degradation of said matrix.

***Claim Rejections - 35 USC § 112 2<sup>nd</sup> Paragraph***

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 12, 13, 15 – 17, 21, 23, 25, 26, 28 and 29 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Non-polymeric chains that possess certain properties can be grafted to the polymer of natural origin in the matrix material. Among the examples provided for non-polymeric grafted chains that possess the property of inhibiting reactions of degradation of said matrix are enzymes (p 8, ln 21 – 23). However, enzymes can either be protein (amino acid polymer) based or RNA (nucleotide polymer) based (also known as ribozymes). Therefore, it is unclear what applicant means by non-polymeric chains having properties for inhibiting reactions of degradation of said matrix as one genera exemplified as belonging to this category is polymeric in nature.

9. Claims 15 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which

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applicant regards as the invention. These claims add limitations on the amount of cross linkage in the matrix material. One quantity to use in the determining the amount of cross linkage is “the number of moles of the cross linking agent ensuring the linking of the polymer chains”. It is unclear from this language and the examples provided in the specification what quantity this represents. For example, it could represent the total amount of cross linking agent, not all of which generally reacts with the polymer, or a determination of how much of the excess amount of cross linking agent did in fact react to link polymer chains together that has been measured in some way.

10. Claims 16, 17, 23, 25, 26, 28 and 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite additional components that must be contained in the matrix. However, the categories presented for the additional components overlap and it is unclear how many distinct components and what properties those components must have (or not have) to be placed in a particular group. For example, claims 16, 23 and 25 require antioxidants agents, vitamins and other dispersed pharmacologically active agents. Vitamin C (ascorbic acid) is one example of a compound that is both a vitamin and an antioxidant agent and therefore could be placed in either or both categories. Would a vitamin have to possess no antioxidant properties in order to be placed in the vitamin category? And while “dispersed” is only used in association with the category “other dispersed pharmacologically active agents”, there is an implication that the antioxidants and

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vitamins are also dispersed. As the non-polymeric grafted side chain can also be antioxidant, it is unclear whether both covalently attached and non-covalently attached (dispersed) antioxidants must be present in the matrix material.

### ***Claim Rejections - 35 USC § 103***

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

12. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

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not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 12, 13 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nguyen (EP 0 749 982 A1).

Nguyen disclosed grafted polysaccharide compositions wherein the grafted side chains are antioxidants (abstract). Preferably the polysaccharides are hyaluronic acids (HLA) or crosslinked HLA that have been grafted with hindered phenols (p 2, ln 3 – 4). Grafting with antioxidants increases the resistance of the polysaccharide to hydroxy radicals (p 2, ln 37 – 38), one cause of degradation of these materials when they are introduced into the body in spaces such as the synovial cavity (p 2, ln 18 – 19). The crosslinking of the polysaccharide can be accomplished in a number of ways, including crosslinking HLA with bi- or polyfunctional epoxides or their corresponding halohydrins, epihalohydrins or halides and divinyl sulfones (p 4, ln 50, ln 56 – 58). A grafting level of 1 equivalent of antioxidant to 10 equivalents of polysaccharide repeating units, or 10% grafting, is disclosed (p 5, ln 16 – 17).

Nguyen does not explicitly prepare an example in which crosslinked HLA is grafted with a non-polymeric side chain having antioxidant properties.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to prepare a matrix material comprised of crosslinked HLA with non-

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polymeric sides with antioxidant properties as all the elements are well taught by Nguyen even though an example of such a matrix material is not prepared.

15. Claims 12, 13, 16, 23, 26 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nguyen as applied to claims 12, 13 and 17 above, and further in view of Ramamurthi et al. (J Biomed Mater Res 2002).

Nguyen discloses crosslinked HLA polymeric materials in which compounds having antioxidant activity are grafted onto the polymer. The crosslinked grafted HLA can be used as a drug delivery system as it forms a molecular cage in which molecules with pharmacological activity can be dispersed (p 7, ln 20 – 30). The drug or mixture of drugs may be covalently or non-covalently bound to the matrix material. The gels films, threads, particles or sponges of HLA-based composition can be placed, sprayed, ingested, injected or implanted at the location where the contained pharmacological substance is needed (p 7, ln 26 – 30).

Nguyen discloses that a mixture of drugs can be contained in the matrix but does not explicitly disclose a matrix material in which vitamins, antioxidant agents and other dispersed pharmacologically active ingredients are all present in the matrix material.

Ramamurthi et al. uses divinyl sulfone crosslinked HLA-based polymers (referred to as hylans) and that crosslinking imparts structural strength and greater permanence to the matrix material (abstract, p 196, col 2, paragraph 1). These properties are needed when using this material as a cell scaffold for tissue engineering applications. When this material was seeded with cells, a small amount of DMEM-F12 with fetal bovine serum

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(FBS) and streptomycin sulfate was added (p 198, col 1, paragraph 3). The materials present in the media were able to enter the hylan material and the resulting matrix contains all the elements present in the media. A large number of components are present in DMEM-F12, including the antioxidant cysteine; the vitamins folic acid, pyridoxal HCl, pyridoxine HCl, riboflavin, thiamine HCl and vitamin B12; and linoleic and lipoic acid, two substances that possess pharmacological activity (HyClone media formulation for Dulbecco's Modified Eagle's Medium/Nutrient Mixture F-12, accessed 4/29/08).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to prepare a antioxidant grafted, crosslinked HLA polymer as taught by Nguyen and add vitamins, antioxidants and other pharmacologically active ingredients as Ramamurthi et al. teaches that crosslinked HLA matrices can be prepared which contain a large number of active ingredients.

16. Claims 12, 13, 15 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nguyen as applied to claims 12, 13 and 17 above, and further in view of Bolotin (PGPub 2003/0224974).

Nguyen discloses crosslinked HLA polymeric materials in which compounds having antioxidant activity are grafted onto the polymer. For injection of these materials, a solution with a sufficient viscosity is prepared that so as to pass through the injection needle, generally between 5,000 cps and 50,000 cps.

Nguyen does not disclose variations in the amount of crosslinking present depending on the final product to alter the viscosity or physical properties in general depending on the type of material (injectable or solid) being produced.

Bolotin discloses that the physical properties of polymers can be adjusted by altering the chemical components and crosslinking using methods familiar to practitioners of ordinary skill in the art (paragraph [0188]). A higher amount of crosslinking results in a more rigid product.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to alter the amount of crosslinking present in the crosslinked antioxidant grafted HLA matrix taught by Nguyen as Bolotin teaches that such manipulations alter the physical properties of the polymer and is within the skill of one of ordinary skill in the art. The amount of crosslinking is a results effective parameter. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ and reasonably would expect success. It would have been customary for an artisan of ordinary skill to determine the optimal amount of crosslinking and therefore physical properties of the matrix material depending on the intended use.

17. Claims 12, 15, 25 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nguyen and Bolotin, further in view of Ramamurthi et al.

Nguyen et al. discloses a matrix material of crosslinked HLA with antioxidant grafted chains. Bolotin discloses that the physical properties of the polymer can be altered by altering the amount of crosslinking present.



Neither Nguyen nor Bolotin disclose a mixture of drugs can be contained in the matrix but does not explicitly disclose a matrix material in which vitamins, antioxidant agents and other dispersed pharmacologically active ingredients are all present in the matrix material.

Ramamurthi et al. uses divinyl sulfone crosslinked HLA-based polymers (referred to as hylans) and that crosslinking imparts structural strength and greater permanence to the matrix material (abstract, p 196, col 2, paragraph 1). These properties are needed when using this material as a cell scaffold for tissue engineering applications. When this material was seeded with cells, a small amount of DMEM-F12 with fetal bovine serum (FBS) and streptomycin sulfate was added (p 198, col 1, paragraph 3). The materials present in the media were able to enter the hylan material and the resulting matrix contains all the elements present in the media. A large number of components are present in DMEM-F12, including the antioxidant cysteine; the vitamins folic acid, pyridoxal HCl, pyridoxine HCl, riboflavin, thiamine HCl and vitamin B12; and linoleic and lipoic acid, two substances that possess pharmacological activity (HyClone media formulation for Dulbecco's Modified Eagle's Medium/Nutrient Mixture F-12, accessed 4/29/08).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to prepare a antioxidant grafted, crosslinked HLA polymer as taught by Nguyen and add vitamins, antioxidants and other pharmacologically active ingredients as Ramamurthi et al. teaches that crosslinked HLA matrices can be prepared which contain a large number of active ingredients and the physical properties of the matrix

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can be altered by altering the amount of crosslinking present in the polymer as taught by Bolotin.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nissa M. Westerberg whose telephone number is (571)270-3532. The examiner can normally be reached on M - F, 8 a.m. - 4 p.m. ET. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/  
Supervisory Patent Examiner, Art Unit 1618

NMW

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